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TRIGGER-SPECIFIC RISK FACTORS FOR CARDIAC EVENTS IN PATIENTS WITH THE CONGENITAL LONG-QT SYNDROME TYPE 2

ACC Poster Contributions
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Authors: *James A. Kim, Arthur J. Moss, Coeli M. Lopes, Scott McNitt, Jennifer L. Robinson, Wojciech Zareba, Ilan Goldenberg, University of Rochester Medical Center, Rochester, NY*

Background: Cardiac events occur in a gene-specific manner among patients with the congenital long-QT syndrome (LQTS). Mutations in the HERG channel in patients with long-QT syndrome type-2 (LQT2) have been shown to be associated predominantly with arousal and exercise-induced triggers. We hypothesized that clinical and genetic risk factors for cardiac events in the LQT2 population are trigger-specific.

Methods: Cox proportional hazards regression modeling was employed to evaluate trigger-specific risk factors for cardiac events among 422 genetically-confirmed LQT2 patients from the US portion of the International LQTS Registry.

Results: One hundred and forty two study patients experienced a cardiac event, of whom 51 (36%) were associated with arousal triggers, 23 (16%) were associated with exercise triggers, and 68 (48%) were associated with non-arousal/non-exercise triggers. In the arousal group, 34% of patients had transmembrane (TM) mutations and 24% had mutations in the Per-Arnt-Sim (PAS) region, whereas in the exercise group 70% had TM mutations and none had PAS mutations. Multivariate analysis demonstrated that female sex, QTc duration, and mutations in the TM and PAS regions were associated with increased risk for arousal-triggered events, whereas TM mutations dominated the risk for exercise-triggered events (Table).

Conclusion: Our findings indicate that specific clinical and genetic risk factors contribute to arousal-triggered cardiac events in patients with the LQT2 genotype.

Table

Event Trigger	Acute Arousal		Exercise		Non-Arousal/Non-Exercise	
Variable	HR	P-value	HR	P-value	HR	P-value
Female:Male	2.49	0.002	1.16	0.673	1.45	0.100
QTc≥500 msec:QTc<500 msec	1.64	0.034	1.23	0.563	1.74	0.013
TM:Non-TM	1.7	0.045	3.7	0.003	1.55	0.068
PAS:Non-TM	1.61	0.097	NA*		1.11	0.719
*No patients with exercise triggers had PAS mutations Findings were adjusted for treatment with beta-blocker therapy						